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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,273	04/13/2001	James R. LaDine	12800-003001	4611

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EXAMINER	
BORIN, MICHAEL L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,273	LADINE ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-18 and 22-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-18 and 22-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Brief on Appeal filed 03/21/2005 is acknowledged.

Upon further consideration of the prior art used in the course of the prosecution of this application, it was deemed necessary to modify the way they have been used in the rejections. Consequently, the finality of the previous Office action is withdrawn.

Claims 1,2,5-18, 22-45 are pending.

2. The following new grounds of rejection are applied.

Claim Rejections - 35 USC § 102 and 103.

3. Claims 1,2,6,7,9-18,22,36,37,43-45 are rejected under 35 U.S.C. 103(a) as obvious over Chang et al (US 4507555).

Chang describes parallel mass spectrometer which consists of two or more sets of ion extraction means, mass resolution devices and ion detectors connected in parallel and interfaced with a computer. See abstract and Fig. 1. Chang does not directly teach using parallel mass spectrometer for multiple samples; however, the reference clearly suggests such use. Thus, the reference discusses that in the GC-MS analysis there may be a complex sample which may consist of hundreds of components (col. 3, lines 27-31). Further, the reference teaches that in GC-MS experiment there may be a complex sample which may consist of hundreds of components (col. 4, lines 27-30), and that in a typical repetitive mass spectra acquisition operation, during an one-hour period of GC run, as many as 3600 might need to be acquired, processed and stored in

a computer system (col. 2, last paragraph). Thus, it would be obvious to one skilled in the art at the time the invention was made that using the parallel mass spectrometer described in Chang for the analyzing multiple samples, which is the intended use of GC-MS spectrometer, one would measure multiple samples (i.e. taken at different time points), having multiple components, and using multiple mass spectrometry systems (i.e. two sets of ion extraction means, mass resolution devices and ion detectors connected in parallel as described in Chang). Further, such method will inevitably measure both identity of a component (position of mass spectra peak) and its abundance (which follows from the amplitude of mass spectra peak). Thus, use of the parallel mass spectrometer described in Chang for the intended purpose of chromato-mass spectrometry discussed in the Background section, would render the method as instantly claimed.

Further, with respect to analyzing proteins as a particular type of components of a biological system, the reference teaches use of parallel mass spectrometer in general without specifying chemical nature of the components. However, in the absence of evidence to the contrary, it would be obvious to select a biological system of interest and to measure components of said biological system.

Further, as the parallel mass spectrometer described in Chang is connected to a computer, it is obvious that such device will be capable of displaying results in the manner claimed in claim 2 or 45.

With respect to claims 6,7, the reference is silent about the exact amount of components, but teaches that in GC-MS experiment there may be a complex sample which may consist of hundreds of components. Col. 4, lines 27-30.

With respect to claims 12,17,18,36, selection of methods of preparing samples and selecting appropriate time intervals of sampling would be obvious to an artisan as a part of routine optimization.

With respect to claims 9,13,37 although the reference addresses combination of MS with GC (gas chromatography), it states that gas chromatography is just an example of separation device (see Abstract), and it would be obvious to an artisan that any equivalent type of separation chromatography, liquid chromatography for example, can be used instead of gas chromatography. See col. 1, last full paragraph , for example.

With respect to claims 14-16,22,43,44, it would be obvious to an artisan that measurement of a time course of changes in biological system can be made in response to exposure of the biological system to a stimulus.

Therefore it would be obvious to apply parallel mass spectrometry to any problem requiring multiple measurements of samples containing plurality of components, such as, for example, measurement of plurality of proteins from a quiescent or stimulated biological sample.

The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in

the art, established scientific principles, or legal precedent established by prior case law. Further, the rationale to support a rejection under 35 U.S.C. 103 may rely on logic and sound scientific principle. "In considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom". In re Prada , 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968).

4. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Chang et al (US 4507555).

Chang et al. as discussed above, describes parallel mass spectrometer which consists of two or more sets of ion extraction means, mass resolution devices and ion detectors connected in parallel and interfaced with a computer.

5. Claims 1,2,5-18,22-45 are rejected under 35 U.S.C. 103(a) as obvious over Demirev et al. (Analytical Chemistry (1997), 69(15), 2893-2900) in view of Chang et al (US 4507555).

The instant claims are drawn to method of analysis of plurality of proteins obtained from a biological system. The method comprises steps of separating multiple protein samples, analyzing them with parallel mass spectrometry and correlating mass spectrometry data as a function of time.

Demirev et al explore feasibility of a "massively parallel" mass spectrometry of proteins and suggests that practical implementations of parallel mass spectrometry

seem feasible for protein libraries containing from several hundreds to several thousand individual components, or for monitoring the diversity of up to a thousand reaction products. See p. 2900, last two paragraphs. In their theoretical analysis, Demirev et al assume multiple separation of components but intentionally do not dwell into details of mass spectrometry arrangement (p. 2898, right column), but mention that there is a number of instrumental factors that must be accounted for in practical implementation of "parallel" mass spectrometric approach, such as e.g., detection efficiency and accuracy of mass spectrometry.

Chang et al., in the Background section[1] teaches that chromatography/mass spectrometry separation may utilize a complex sample which may consist of hundreds of components (col. 4, lines 27-30), and that measuring large amount of samples produces a huge amount of information and that repetitive mass spectra acquisition operation may cause spectrum distortion and large amount of data in high resolution chromatography/mass spectrometry places enormous demand on the interfaced computer capability and is rarely possible (col. 2, bottom). Chang describes that when interfaced with a sample separation device, such as gas- or liquid- chromatography system, parallel mass spectrometer can provide a significant advantage over conventional single mass spectrometer, for example, in terms of resolution and sensitivity (col. 1, last full paragraph).

It would be *prima facie* obvious at the time the invention was made that successful "massively parallel" mass spectrometry of proteins discussed in Demirev et

[1] i.e., specifics of device which is the subject of invention of Chang et al is not addressed in this rejection

al may require not only multiple separation devices, bur also parallel mass spectrometers, because Demirev addresses difficulties in practical implementation of "massively parallel" mass spectrometry for detection, such as efficiency and accuracy, and Chang et al, also discussing difficulties in mass spectral identification of complex mixtures of ingredients, point to parallel mass spectrometer as being able to provide a significant advantage over conventional single mass spectrometer, for example in terms of resolution and sensitivity. An artisan would have a reasonable expectation of success in using parallel mass spectrometry system because they will be at least as effective as, and most likely better than, single mass spectrometry system. Further, it would be obvious to an artisan to determine and optimize all parameters of separation, such as numbers of separation and detection systems, and other result-oriented conditions of separation and detection. If there are any differences between the dependent claims Applicant's claimed method and that of the prior art, the differences would be appear minor in nature. Although the prior art do not teach all particular combinations of limitations of the method as claimed, selection of optimal parameters would be conventional and within the skill of the art of analytical biochemistry. See discussion of limitations of dependent claims on the rejection over Chang et al. above.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Mr. Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

May 19, 2005

mlb